

## REMARKS

Claims 1-107 were pending in the present application.

Applicants have amended claims 1, 23, 39, 42, 81-90, and 105 to clarify that which Applicants regard as the invention. Specifically, claims 1, 23, and 81-90 have been amended to specify that the antibody or a fragment thereof comprises a variable domain that specifically binds to the extracellular domain of native Fc $\gamma$ RIIB. Claims 39 and 42 have been amended to specify that the antibody or fragment thereof comprises a variable domain that (i) competes for binding with the specified antibody, and (ii) binds Fc $\gamma$ RIIB with greater affinity than said antibody or fragment thereof binds Fc $\gamma$ RIIA. Support for these amendments can be found in the specification, for example, at page 20, lines 16-20, and page 29, lines 7-8. Claim 105 has been amended to recite that the Fc region has an altered affinity for an Fc $\gamma$ R. Support for this amendment can be found in the specification, for example, at page 36, lines 31-32.

Applicants have added new claims 108-109 directed to additional embodiments of the invention. Specifically, claim 108 is directed to antibodies of claim 1 comprising a variable domain which specifically binds to Daudi cells. Claim 109 is directed to antibodies of claim 1 comprising a variable domain which does not specifically bind denatured Fc $\gamma$ RIIB. Support for these new claims can be found in the specification, for example, at page 12, lines 12-18, page 20, lines 16-20, and page 60, lines 6-15.

No new matter has been added by these amendments.

Applicants respectfully request entry of these amendments. After entry of the amendments, claims 1-109 will be pending.

## Elections/Restrictions

The Examiner has alleged that the application contains the following inventions or groups of inventions and has required Applicant to elect a single invention:

I. Claims 1-8, 16-21, 23, 27-32, 34, 36-43, 81-90, 104-107, drawn to an isolated antibody or a fragment thereof that specifically binds native Fc $\gamma$ RIIB with greater affinity wherein the binding agonizes at least one activity of Fc $\gamma$ RIIB.

**II.** Claims 1, 9-21, 23, 27-32, 34, 36-43, 81-90, 104-107, drawn to an isolated antibody or a fragment thereof that specifically binds native Fc $\gamma$ RIIB with greater affinity wherein the binding antagonizes at least one activity of Fc $\gamma$ RIIB.

**III.** Claims 22, and 24-26, drawn to a bispecific antibody that binds Fc $\gamma$ RIIB and a tumor antigen.

**IV.** Claims 33, 35, 91 and 92, drawn to a method of producing a monoclonal anti-Fc $\gamma$ RIIB antibody by immunizing Fc $\gamma$ RIIA transgenic mice.

**V.** Claims 44-50, drawn to an isolated nucleic acid encoding agonizing anti-Fc $\gamma$ RIIB antibody, a vector, a host cell and a method of producing the antibody.

**VI.** Claims 44-50, drawn to an isolated nucleic acid encoding antagonizing anti-Fc $\gamma$ RIIB antibody, a vector, a host cell and a method of producing the antibody.

**VII.** Claims 51-59, 77, and 93-103, drawn to a method of treating cancer characterized by a cancer antigen comprising administering antibody that specifically binds Fc $\gamma$ RIIB and a second antibody.

**VIII.** Claims 60-64, drawn to a pharmaceutical composition comprising an anti-Fc $\gamma$ RIIB antibody, an antibody specific for cancer antigen and a carrier.

**IX.** Claims 65-72, 75, and 76, drawn to a method of treating an autoimmune disorder by administering an antibody specific for Fc $\gamma$ RIIB.

**X.** Claims 73-76, drawn to a method of treating or preventing an IgE-mediated allergic disorder by administering an antibody specific for Fc $\gamma$ RIIB.

**XI.** Claims 78 and 79, drawn to a method of diagnosis of an autoimmune disease.

**XII.** Claim 80, drawn to a method of enhancing an immune response to a vaccine composition by administering an antibody specific for Fc $\gamma$ RIIB and a vaccine composition.

**XIII.** Claims 96, 97, 100-103, drawn to a method of treating a disease by administering an antibody specific for Fc $\gamma$ RIIB and a non-cell killing antibody.

The Examiner also alleges that the application contains claims directed to more than one species of the generic invention, as set forth below:

If any one of the Groups I-XIII is elected, applicant is required to elect:

- (a) one specific antibody produced by a specific hybridoma, AND
- (b) which, if any, of the functional limitations recited are encompassed by the elected antibody species.

In addition, if any one of Groups I and II is elected, applicant is required to elect one specific antibody:

- (a) without conjugation, OR
- (b) conjugated to one specific therapeutic agent.

If any one of Groups III, VII, and VIII is elected, applicant is further required to elect and ultimate species wherein the second heavy-light chain pair binds to:

- (a) one specific tumor antigen, AND
- (b) one specific cancer as it reads on the elected tumor antigen species.

If Group IX is elected, applicant is further required to elect method of treating

- (a) one specific autoimmune disorder (e.g. rheumatoid arthritis), AND
- (b) administering specific immunomodulatory agents.

If Group X is elected, applicant is further required to elect a method of treating one specific disease (e.g. asthma).

If Group XI is elected, applicant is further required to elect a method of diagnosis using one specific detectable marker.

If Group XIII is elected, applicant is further required to elect a method of treating by administering one specific second non-cancer-antigen-binding antibody (e.g. anti-Fas antibody).

The Examiner alleges that the invention of Groups I-II have no special technical feature that defined a contribution over Presta (U.S. Patent Application No. 2004/0191244). Specifically, the Examiner alleges that Presta teaches methods of making an antibody with altered effector functions by replacing amino acids in the Fc receptor binding

sites of an antibody Fc region which may increase the binding affinity to Fc receptors including Fc $\gamma$ RIIB.

Applicants respectfully traverse the Restriction Requirement with respect to groups I-II and respectfully assert that the restriction of groups I-II is improper under 35 U.S.C. §121.

Applicants note that claims 36-43 belong to Group II.

The Examiner has cited Presta as support that the invention of Groups I-II have no unifying, novel technical feature. Applicants respectfully disagree. Presta is directed to modifications to the Fc region of antibodies to alter binding of the Fc region to an Fc $\gamma$ R. Fc receptors bind the Fc region of an antibody, and the Fc region is not directly involved in binding the antigen against which the antibody is directed. See Presta, e.g., Fig. 1, [0007]-[0008] and [0013]. It is the variable domains of the antibody that are responsible for binding of the antibody to an antigen. See id. at [0006]. In contrast, the present invention is directed to native human Fc $\gamma$ RIIB-specific antibodies which specifically bind to Fc $\gamma$ RIIB as the antigen, i.e., the variable domain of the claimed antibody binds specifically to Fc $\gamma$ RIIB. This is completely distinct from what Presta teaches. Thus, the inventions of Group I-II have a special technical feature over Presta. Accordingly, Applicants respectfully request that Groups I-II be joined.

However, in order to be fully responsive, Applicants are provisionally electing, with traverse, to prosecute the claims in group II directed to an isolated antibody or a fragment thereof that specifically binds native Fc $\gamma$ RIIB with greater affinity wherein the binding antagonizes at least one activity of Fc $\gamma$ RIIB, and have elected as a species, the antibody 2B6, which has the functional limitations recited in claims 9-15, and without conjugation. Applicants believe that claims 1, 9-20, 23, 30-32, 38, 41-43, 81-90, and 104-109 read on the elected species.

Attorneys for Applicants retain the right to petition from the restriction requirement under 37 U.S.C. § 1.144.

**CONCLUSION**

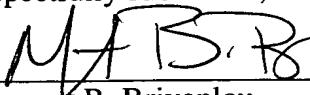
Entry of the amendments and remarks made herein is respectfully requested.

The Examiner is invited to contact the undersigned with any questions concerning the foregoing.

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Respectfully submitted,

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